Adagrasib + SRS for Patients With Metastatic KRAS G12C-mutated NSCLC With Untreated Brain Metastases

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Written informed consent and HIPAA authorization for release of personal health information prior to registration. NOTE: HIPAA authorization may be included in the informed consent or obtained separately. 2. Age ≥ 18 years at the time of consent. 3. ECOG Performance Status of 0-1 within 28 days prior to registration. 4. Confirmation of stage IV non-small cell lung cancer (NSCLC) per AJCC, 8th edition, or metastatic recurrence after treatment for earlier stage disease. 5. Known to have a KRAS G12C mutation. KRAS G12C mutation can be determined based on local tissue and/or ctDNA testing. 6. Presence of brain metastases that meet the following criteria: * Patients must have at least 1 untreated enhancing intracranial lesion, per local radiology interpretation, measuring at least 2mm. NOTE: intracranial lesions do not need to be measurable by RECIST 1.1 criteria to be eligible. * Must have no single metastasis measuring larger than 3 cm. * Patients with surgically resected brain metastases are eligible provided there are additional brain metastases amenable to SRS * Patients with progression of previously radiated or surgically resected CNS metastases are eligible if solid component of lesion has enlarged and there is no concern for radionecrosis based on investigator discretion. * Patients who received SRS within 4 weeks prior to registration are eligible provided baseline brain MRI prior to SRS treatment is within 4 weeks of study registration and SRS treatment meets requirements in #7 below. * Symptomatic brain metastases are permitted if the following criteria are met: * No evidence of cerebral herniation or symptomatic leptomeningeal disease * No seizures within past 14 days; antiepileptic medications are permitted * Patients on steroids must have stable or improving neurologic symptoms that have not worsened during a steroid taper. Must be receiving the equivalent of dexamethasone 8 mg total daily dose or less at the time of registration. 7. CNS lesions have already been treated with SRS (within 3 weeks prior to Cycle 1 Day 1) or are amenable to SRS as determined by radiation oncologist and/or neurosurgeon. SRS treatment must use GammaKnife or linear accelerator-based treatments with nominal x-ray energy of 6MV or greater. 8. No contraindications to SRS. Patients on anticoagulation must be able to hold anticoagulation for SRS treatment based on investigator discretion. 9. Patients may be treatment-naïve OR have received up to 2 prior lines of systemic therapy. Treatment with systemic therapy for Stage I-III disease \> 12 months prior to development of metastases do not count as a line of therapy. Treatment with platinum-doublet chemotherapy and checkpoint inhibitor immunotherapy (PD-1, PD-L1, CTLA-4, etc.) either in combination or sequentially counts as one line of therapy. 10. Demonstrate adequate organ function as defined below. All screening labs to be obtained within 28 days prior to registration. * Hemoglobin (Hgb): ≥ 8.0 g/dL in the absence of transfusions within 7 days prior to testing. * Calculated creatinine clearance: ≥ 60 mL/min * Bilirubin: ≤ 1.5 mg/dL * Aspartate aminotransferase (AST): ≤ 3.0 × ULN * Alanine aminotransferase (ALT): ≤ 3.0 × ULN 11. Females of childbearing potential must have a negative urine or serum pregnancy test within 7 days prior to treatment initiation. 12. Females of childbearing potential who are sexually active with a male able to father a child must be willing to abstain from heterosexual activity or to use an effective method(s) of contraception. Males able to father a child who are sexually active with female of childbearing potential must be willing to abstain from heterosexual activity or to use an effective method(s) of contraception. 13. HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of registration are eligible for this trial. Testing is not required at screening unless mandated by local policy. 14. Patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, the HCV viral load must be undetectable to be eligible for this trial. Testing is not required at screening unless mandated by local policy. 15. As determined by the enrolling physician or protocol designee, ability of the subject to understand and comply with study procedures for the entire length of the study.

Exclusion Criteria:

1. Prior treatment with KRAS G12C tyrosine kinase inhibitor. 2. Active infection requiring systemic therapy with the exception of #13 and #14 above. 3. Uncontrolled, significant intercurrent or recent illness. 4. Prolonged QTc interval \> 480 milliseconds or history of congenital Long QT Syndrome 5. Currently receiving radiation treatment at the time of enrollment to any extra-cranial lesion for prophylaxis or pain control. Patients may enroll after completion of palliative RT. 6. Ongoing need for treatment with concomitant medication known as a strong inhibitor or inducer of CYP3A enzyme and that cannot be switched to an alternative treatment prior to study enrollment. NOTE: Discontinuation of CYP3A4 inducers should occur a minimum of 7 days or 5 times their half-life, whichever is longer, prior to C1D1 study treatment. 7. Treatment with any investigational drug within 28 days prior to registration. 8. Pregnant or breastfeeding (NOTE: breast milk cannot be stored for future use while the mother is being treated on study). 9. Patients with a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the investigational regimen, per treating physician discretion, are not eligible for this trial.

Conditions & Interventions

Interventions:
DRUG: Adagrasib, RADIATION: Stereotactic Radiosurgery
Conditions:
Non Small Cell Lung Cancer, NSCLC, KRAS G12C

More Information

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